REMARKS

Claims 1, 10-13 and 42-45 are pending in the subject application. By this Amendment, applicants have amended claims 10-13, 42 and 44, and have added new claims 47-52. Support for amended claims 10-13 may be found in the specification *inter alia* at page 14, lines 24-29. Support for new claims 47 and 48 may be found at page 14, line 29 to page 15, line 3. Support for new claims 49 and 50 may be found at page 15, lines 25-27. Support for new claims 51 and 52 may be found at page 16, lines 4-5. Applicants maintain that amended claims 10-13 and 42, and new claims 47-52 do not raise an issue of new matter and request that this Amendment be entered. Accordingly, upon entry of this Amendment, claims 1, 10-13 and 42 as amended, and claims 43-45 and 47-52 will be pending and under examination.

Double Patenting Rejections

Rejection Under 35 U.S.C. §101

In the November 28, 2006 Advisory Action, the Examiner indicated that the rejection of claim 46 under 35 U.S.C. §101 as allegedly claiming the same invention as that of claim 3 of prior U.S. Patent No. 6,692,745 B2 is moot in view of the cancellation of claim 46.

Rejection Under Obviousness-Type Double Patenting

The Examiner maintained the rejection of claims 1, 10-13 and 42-45 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-15 of U.S. Patent No. 6,692,745 B2 for reasons of record. As the Examiner has noted, applicants have indicated they might consider filing a terminal disclaimer later in prosecution if allowable claims are indicated and the rejection is applicable thereto.

Rejections under 35 U.S.C. §103(a)

The Examiner maintained the rejection of claims 1, 10-13 and 42-45 under 35 U.S.C. §103(a) as allegedly "unpatentable over Allaway et al. (5,817,767; 'Allaway') in view of Bolognesi et al. (5,464,933;

'Bolognesi')." The Examiner stated that the U.S. Patent Office maintains its position that T-20 and Allaway's antibody are functional equivalents.

In the November 28, 2006 Advisory Action, the Examiner indicated that (1) although the actual mechanism of inhibiting fusion is different, the ultimate functional outcome is the same, and thus, one of ordinary skill in the art would have been motivated to substitute T-20 for Allaway's antibody; and (2) there is a reasonable expectation of success when using T-20 in combination with an anti-gp120 antibody for inhibiting HIV infection. The Examiner stated that Allaway discloses the synergism associated with targeting gp120 and gp41 in combination.

In response, applicants respectfully traverse the Examiner's ground of rejection.

Applicants' invention as recited in the amended and new claims set forth above provides methods which utilize two peptidyl compounds, wherein one compound is a monoclonal antibody or a portion thereof which retards attachment of HIV-1 to a CD4+ cell by retarding binding of HIV-1 gp120 envelope glycoprotein to CD4 on the surface of the CD4+ cell and the other peptidyl compound is a peptide designated T-20 (SEQ ID NO:1) which retards gp41 from adopting a conformation capable of mediating fusion of HIV-1 to a CD4+ cell by binding noncovalently to an epitope on a gp41 fusion intermediate, wherein the relative mass ratio of the compounds ranges from about 100:1 to about 1:100, including the use of compositions comprising an admixture of such two compounds and such compositions *per se*.

Allaway discloses the use of two peptidyl compounds to inhibit HIV-1 infection. For purposes of this response, applicants focus on the following:

1. the differences between the antibody of Allaway which inhibits fusion and the peptide T-20 recited in applicants' claims, and the unobviousness of using the T-20 peptide;

2. the unexpected superiority attributable to the two peptidyl

compounds recited in applicants' claims relative to the two peptidyl compounds in Allaway; and

3. the lack of any disclosure whatsoever in Allaway of a peptidyl compound which binds to an epitope of CD4 on the surface of a cell, including any such antibody or portion thereof as recited in applicants' new claims 51 and 52.

1. The Differences Between The Antibody Of Allaway and T-20 And The Unobviousness Of Using The T-20 Peptide

a. The Allaway Antibody

The antibody disclosed by Allaway binds to an epitope on gp41 which is present on the viral envelope surface prior to gp41 undergoing a conformational change to the prehairpin fusion intermediate of gp41 which exposes the gp41 epitope to which T-20 binds. The antibody of Allaway binds a conserved epitope on gp41 which is transiently exposed prior to fusion of HIV-1 to a CD4+ cell.

The specific anti-gp41 antibody 2F5 disclosed by Allaway at column 5, lines 32-38 and column 8, lines 48-54, and antibodies similar to 2F5 disclosed by Allaway at column 14, lines 44-67 to column 15, lines 1-15, are directed "to a conserved epitope of HIV-1 gp41" (See column 10, lines 56-59 and column 16, line 66 of Allaway). Moreover, the 2F5 antibody is directed against and interacts with epitopes on gp41 that are constitutively present on virus particles prior to fusion (See applicants' specification at page 6, lines 11-14).

b. The T-20 Peptide

The T-20 peptide recited in applicants' claims binds to an epitope which is transiently exposed prior to fusion when gp41 assumes the prehairpin conformation. The binding of T-20 to this epitope prevents gp41 from adopting the fusogenic conformation required for fusion of HIV-1 to a CD4+ cell.

c. The Allaway Antibody Is Structurally And Functionally Distinct From The T-20 Peptide. Allaway In View Of Bolognesi Does Not Render Obvious Use Of The T-20 Peptide

First, it is clear that an antibody is structurally distinct from a peptide. Second, the Allaway antibody interacts with an epitope unrelated to the epitope with which T-20 interacts. Third, Allaway does not disclose the existence of any transiently exposed epitope, let alone the epitope to which T-20 binds, nor the fact that fusion can be inhibited by binding to such a transiently exposed epitope. Thus, applicants' claimed invention involving the T-20 peptide is not obvious from the disclosure of Allaway which relates to a structurally distinct and not functional equivalent antibody. Moreover, Allaway certainly does not make it obvious to select the gp41 derived peptide DP-178 which is referred to by applicants as the T-20 peptide given the numerous peptides disclosed by Bolognesi.

Applicants further note that neither Allaway nor Bolognesi disclose what effect, if any, would occur in the event the antibody in the composition disclosed in Allaway was replaced by a peptide as disclosed in Bolognesi. There is no indication in the prior art that a fusion inhibitor that binds to a gp41 prehairpin fusion intermediate could be substituted for an antibody that inhibits fusion by binding to the viral surface glycoprotein gp41. Accordingly, applicants maintain that the Examiner has not properly established a *prima facie* case of obviousness.

2. The Unexpected Superiority Attributable To The Two Peptidyl Compounds Recited In Applicants' Claims Relative To The Two Peptidyl Compounds In Allaway

Applicants further maintain that even if a *prima facie* case of obviousness were properly established, which applicants maintain the Examiner has failed to do, such *prima facie* case is rebuttable by the evidence of unexpected results over the prior art as disclosed in applicants' specification.

Applicants maintain that the synergistic effect of the two compounds recited in their claims is unexpectedly superior to the synergistic effect disclosed in Allaway. As detailed in the specification at page

26, lines 8-10, the degree of synergy resulting from the two compounds was quantified using the Combination Index (CI) method, wherein a CI value greater than 1 indicates antagonism, a CI equal to 1 indicates a purely additive effect, and a CI of less than 1 indicates a synergistic effect. As shown in Figure 2 of the subject application, under optimal conditions, potent synergies over broad ranges of inhibitor ratios and concentrations were observed with CI values as low as 0.20. Specifically, the average CI values for 95%, 90%, and 75% inhibition disclosed in Figure 2 are 0.31, 0.36, and 0.47, respectively. In contrast, the average CI values for 95%, 90%, and 75% inhibition disclosed in Allaway, column 17, Table 2, are 0.50, 0.56, and 0.70, respectively. Accordingly, the synergy attributable to the two compounds recited in applicants' claims is unexpectedly superior to that achieved by the two compounds disclosed in Allaway. Such evidence of unexpected superiority renders applicants' claimed invention unobvious over Allaway in combination with Bolognesi.

3. The Lack Of Any Disclosure Whatsoever In Allaway Of A Peptidyl Compound Which Binds To An Epitope Of CD4 On The Surface Of A Cell, Including Any Such Antibody Or Portion Thereof As Recited In Applicants' New Claims 51 And 52

Allaway discloses a peptidyl compound which retards binding of HIV-1 gp120 glycoprotein to CD4 by binding to gp120. Allaway does not disclose any compounds that retard binding of HIV-1 gp120 glycoprotein to CD4 by binding to an epitope on CD4 on the surface of CD4+ cells. Thus, the rejection over Allaway in view of Bolognesi is not applicable to new claims 51 and 52.

Conclusion

In view of the remarks above, applicants maintain that the pending claims are not obvious over the cited references and respectfully request that the Examiner reconsider and withdraw the ground of rejection under 35 U.S.C. §103. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw these grounds of rejection, and request allowance of all claims pending in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the $395.00 fee for filing an RCE and the $1080.00 for a five-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

8/2/07

John P. White Date
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